

Attorney Docket No. 06969.0028-00  
Patent Application No. 09/335,689

## REMARKS

### I. Status of the Claims

As a preliminary matter, Applicants wish to thank Examiner Schnizer for extending Applicants' representatives telephone interviews on June 19, 2001, and on July 5, 2001.

Applicants respectfully request that the Amendment dated April 4, 2001, not entered previously, be entered in this Continued Prosecution Application.

After entering the Amendment dated April 4, 2001, and the present Amendment, claims 1-4, 6-15, 17-26, and 28-46 are pending in this application. Claims 1, 17, and 25 were amended in order to more clearly define the subject matter of the invention and not to overcome prior art. No new matter has been added by these amendments.

Support for new claims 31-34 can be found in the specification at page 11, lines 16-17, at page 17, lines 6-10, Example 2, and Figures 2-3. Support for new claims 35-38 can be found in the specification at page 18, lines 2-6 and in Figure 1. Support for new claims 39-42 can be found in the specification at page 17, lines 1-5 and Example 3, specifically at page 45, lines 3-7. Support for new claims 43-46 can be found in the specification at page 39, line 4 and Figures 2-3.

Claims 1, 17, and 25, were amended in order to more clearly define the subject matter of the invention in response to the Examiner's indefinite rejection under 35 U.S.C. § 112, second paragraph. Furthermore, the scope of the claims was not intended to be narrowed by these amendments. The claims were simply amended to include the definition of "substantially homogenous" as defined in the specification.

### II. Claim Rejections under § 112

In the Advisory Action dated April 17, 2001, the Office states that the proposed amendments in Applicants' response filed on April 4, 2001, would require micellar complexes wherein the variation in size distribution of the micellar complexes is less than or equal to 20% with respect to the mean size of the micellar complexes. The

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Office argues that it would be unclear whether this limitation allows a total variation of 20%, e.g., 10% above the mean and 10% below the mean or whether it allows a distribution of 20% above the mean and 20% below the mean.

The Office further argues that the specification fails to enable the claim methods of making populations of micellar complexes with the recited variation in size. Applicants understand the Office's position as described below. The complete argument by the Office can be found in the Advisory Action at pages 2-3.

The Office responded to Applicants' arguments (Paper No. 9) in which Applicants directed the Office to examine the size distribution rather than the range in size of the micellar complexes by stating that the Office is looking at the proposed amendment, which recites "the variation in size distribution." The Office states that in Figure 3C complexes are produced which range in size from 0-100 nm, and thus, in the Office's opinion, the size distribution is from 0-100 nm. The Office further states that the apparent average size of these micelles is about 30-40 nm. Therefore, according to the Office, the variation in size distribution (100 nm) exceeds 100% of the mean size of the micelles (30-40 nm).

Applicants respectfully traverse this rejection. Applicants submit that the instant claims recite "variation in *size distribution* of less than or equal to about 20%", and not merely a variation in the size of the micellar complexes. A particle size distribution in this context represents the relative number (in percentage) of micellar complexes present in each of the different size ranges in a sample. See, for example, Perry's Chemical Engineers' Handbook, Mc Graw Hill 6<sup>th</sup> Ed., chapter 21, p. 13, col 2 (1984). That is, a size distribution is composed of both a collection of size ranges and the fraction of the total number of micellar complexes that fall within each size range.

Applicants enclose, for the Office's reference and convenience, copies of relevant sections of the user manual of the light-scattering instrument used to determine the size distributions of Figures 2-4. Specifically, the section titled "Interpretation of Sizing Results" and a one-page discussion of the exponential

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sampling method employed by the instrument in the calculation of the above size distribution are included.

A size distribution is usually characterized by a distribution mean and a standard deviation. See User Guide Photon Correlation Spectroscopy and Electrophoresis, Malvern Instruments p. 4, ¶ 7. In this case, the standard deviation refers to the width of the distribution, and not to the experimental error. *Id.* Therefore, the skilled artisan would recognize that a variation in size distribution of less than or equal to about 20% indicates, not a variation in the size of micellar complexes, but the standard deviation of the micellar complexes about the mean. In other words, the size distribution of the claims refers to a standard deviation of about 20%.

Therefore, Applicants submit that the instant claims reciting a variation in size distribution of less than or equal to about 20% are not indefinite and are fully supported by the specification. Accordingly, Applicants respectfully request that this rejection be withdrawn.

### III. Conclusions

Please grant any extensions of time required to enter this Preliminary Amendment and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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Dated: Draft

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## APPENDIX TO AMENDMENT OF DRAFT

### Amendments to the Claims

1. A method of making micellar complexes comprising:
  - a) combining at least one cationic lipid with a sufficient amount of PEG derivative to produce micellar lipids;
  - b) combining said micellar lipids and at least one biologically active molecule to form said micellar complexes,wherein the variation in size distribution of said micellar complexes is less than or equal to about 20% ~~with respect to the mean size of said micellar complexes.~~
17. A method of delivering a biologically active molecule to a cell of a mammal comprising contacting said cell with a composition comprising a micellar complex, wherein said micellar complex comprises:
  - at least one cationic lipid;
  - at least one biologically active molecule; and
  - a least one PEG derivativeand wherein said micellar complex is part of a group of micellar complexes having a variation in size distribution of less than or equal to about 20% ~~with respect to the mean size of said group of micellar complexes.~~
25. A micellar complex comprising:
  - at least one cationic lipid;
  - at least one PEG derivative; and
  - at least one biologically active molecule;wherein the variation in size distribution of a group of said micellar complexes ~~has a size distribution is~~ of less than or equal to about 20% ~~with respect to the mean size of said micellar complexes.~~

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